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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/884,211 | 06/18/2001 | Robertson Scott Alan | PC10743A | 3787 |

7590 10/02/2003

Paul H. Ginsburg
Pfizer Inc
20th Floor
235 East 42nd Street
New York, NY 10017-5755

EXAMINER

BRANNOCK, MICHAEL T

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1646

DATE MAILED: 10/02/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/884,211

Applicant(s)

ALAN ET AL.

Examiner

Michael Brannock

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 27 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) 1-8, 21-23 and 25-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 9-20 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 18 June 2001 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

Claims 1-8, 21-23, 25-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12, 6/3/03.

Applicant's election with traverse of Group I, the species of SEQ ID NO: 2, claims 9, 10, 12, 13, 17-20, in Paper 6/3/03 is acknowledged. The traversal is on a number of grounds, which have been thoroughly considered but not deemed persuasive. Regarding Applicant's assertion that there are no statutory grounds for the restriction:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) or distinct as claimed (see MPEP § 806.05- §806.05(I)): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by

(A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction.

Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious.

Applicant asserts that there is no evidence for the utility of using the polynucleotide as a probe for diagnostic purposes, thus undermining the distinction between the polynucleotide and a transgenic animal. This argument has been fully considered but not deemed persuasive.

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Applicant is directed to page 22, L28 to page 22, L27 of the instant specification wherein the use of the polynucleotide in diagnostic assays is discussed.

The examiner does not understand Applicant's reasonings on page 4 regarding the distinctiveness of Group I and Group II.

Applicant asserts that relying on the PTO classification system to establish distinctiveness is improper. This argument has been fully considered but not deemed persuasive. The restriction requirement relied on the different classifications to provide evidence of a search burden, not distinctiveness per se. For example, although a search of the polypeptides of Group II would overlap a search of the polynucleotides of Group I, the two searches would not be coextensive. In many instances, a protein will have been known in the art before the DNA has been discovered that encodes the protein. Often the protein will be known by a name different than the name given the protein after the cloning of the nucleic acid - and may even be associated with a completely different activity than that ascribed to it when the nucleic acid was cloned. Thus, for example, groups I and II require divergent searches, and to search both inventions would be burdensome.

Applicant challenges the species restriction requirement. Applicant also notes that SEQ ID NO: 2 is a polynucleotide. The species defined by the examiner are independent and distinct species of invention, one not being required for the use of any other; and although a search of any one of the species may overlap that of another, the search of one species could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of any other species, and to search all species would be burdensome. Therefore, the restriction is

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maintained and made final. Additionally, it is noted that the examiner finds that claims 14 and 15 relate to the elected group and species.

Information Disclosure Statement

Applicant is notified that Paper 4 that was received by the Office on 10/29/2001 indicates that an information disclosure statement (IDS) was provided by Applicant. However, no PTO-1449 or comparable form is now present in the application. Nor are any copies of references, that may have accompanied this form, now present in the application. Applicant is invited to resubmit such for consideration by the examiner.

Sequence Rules Compliance:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: The specification makes reference to specific polynucleotide and/or polypeptide sequences, see page 16, L12 for example; these references must contain a sequence identifier of the form: SEQ ID NO: X. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 10, 17, 18, 19, 20, 24 are rejected under 35 U.S.C. 102(a) as being anticipated by U.S. Patent No: 6100048, filed September 4, 1996.

U.S. Patent No: 6100048 discloses a polynucleotide having 79% sequence identity with the instant SEQ ID NO: 2 over a region of about 1500 base pairs (see attached sequence alignment) and would thus be expected to hybridize to the instant SEQ ID NO: 2 under the conditions required by the claims as highly stringent, absent evidence to the contrary. The polynucleotide disclosed by U.S. Patent No: 6100048 encodes a polypeptide that is a functional melantocortin-4 receptor, see col 14 Example 2F. Vectors, host, cells and methods of producing the polypeptide are also disclosed, see col 15 Example 15.

Claims 9,10, 17, 18, 19, 20, 24 are rejected under 35 U.S.C. 102(a) as being anticipated by WO/00/27863, published May, 18, 2000.

WO/00/27863 discloses a polynucleotide having 87% sequence identity with the instant SEQ ID NO: 2 over a region of about 1000 base pairs (see attached sequence alignment) and

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would thus be expected to hybridize to the instant SEQ ID NO: 2 under the conditions required by the claims as highly stringent, absent evidence to the contrary. The polynucleotide disclosed by WO/00/27863 encodes a polypeptide that is a functional rhesus monkey melantocortin-4 receptor, see the Abstract. Vectors, host, cells and methods of producing the polypeptide are also disclosed, see pages 15-20.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 10, 13-20 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a polypeptide of SEQ ID NO: 3 or 4, and fragments thereof, and fragments thereof with additional heterologous sequences, e.g. epitope tags or carrier proteins, does not reasonably provide enablement polynucleotides encoding polypeptides *comprising* portions of SEQ ID NO: 3 or 4 or which need only hybridize to the encoding polynucleotide under the recited conditions or share a percent identity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 15 and 16 require polynucleotides encoding polypeptides comprising only portions of SEQ ID NO: 4. Also claims 9, 10, 13-20 and 24 require polynucleotides that need only hybridize to the disclosed polynucleotides or share a percent identity. Thus, the vast

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majority of encoded polypeptides are amino acid sequence variants of SEQ ID NO: 4, i.e. amino acid substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 4, yet the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the specification has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID

NO: 4 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 4 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 4 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 4, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 4. Conversely, if a protein variant of SEQ ID NO: 4 need not have a disclosed property, the specification has failed to teach how to use such a variant.

The activities of the polypeptide of SEQ ID NO: 4 depicted in Figs 5-11 were accomplished with expression of the polypeptide of SEQ ID NO: 4. The specification has not provided a working example of the use of a variant of the polypeptide of SEQ ID NO: 4 nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 4 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 4 and still retain any activity of the polypeptide of SEQ ID NO: 4.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 4 that can be

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used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing and screening for active variants (e.g. page 15), this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to generate the infinite number of variant recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 9, 10, 13-20 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a feline and a canine polynucleotide of SEQ ID NO: 1 and 2, respectively, yet the claims encompass polynucleotides not described in the specification, i.e. polynucleotides sequences from other species, mutated sequences, allelic variants, or sequences need that need only hybridize to SEQ ID NO: 1 or 2 under the recited conditions or share a percent identity and yet which retain any useful functional limitations. The specification contemplates these variants, see pages 15 and 16 for example; yet none of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. The skilled artisan would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polynucleotide from a cat and a single polynucleotide from a dog, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, only two naturally occurring polynucleotide sequences, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

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With the exception of the cat and dog polynucleotides referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants that are not encoded by SEQ ID NO: 1 or 2, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the cat and dog polynucleotides, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 9-20 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ novel nucleic acid molecules (i.e. ATCC #s PTA-1762 and PTA-1761).

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Since the nucleic acid molecules are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public.

If the nucleic acid molecules are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the nucleic acid molecules. The specification does not disclose a repeatable process to obtain the nucleic acid molecules and it is not apparent if the nucleic acid molecules are readily available to the public. It is noted that Applicant has deposited the nucleic acid molecules (page 16), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
- (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
- (d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and
- (e) the deposit will be replaced if it should ever become inviable. Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the

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deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination.”

At page 16, the date of the deposit and the address of the depository are missing. The specification should be amended to include such, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 10, 17-20, 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require a “functional MC4R”, yet the specification does not set forth a definition of this term such that the artisan would unambiguously know whether he or she was in possession of a molecule meeting the limitations of the claim. Must a “functional MC4R” have each of the functions depicted in Figs 5-11, or only some? Perhaps a “functional MC4R” is only a small portion of the protein that is capable of eliciting an immune response, e.g. page 41.

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Thus, the artisan cannot be reasonably appraised of the metes and bounds of the claims because of the presence of this term.

Conclusion

No claims are allowable.

Please note the new official fax number below:


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB


September 28, 2003


YVONNE EYLER, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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Sequence alignment: U.S. Patent No: 6100048

APPLICATION NUMBER: US/08/706,281A
FILING DATE: 04-SEP-1996
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: No. 6100048nan, Kevin E
REGISTRATION NUMBER: 35,303
REFERENCE/DOCKET NUMBER: 96,886
TELECOMMUNICATION INFORMATION:
TELEPHONE: 312-913-0001
TELEFAX: 312-913-0002
TELEX:
INFORMATION FOR SEQ ID NO: 15:
SEQUENCE CHARACTERISTICS:
LENGTH: 1671 base pairs
TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: cDNA to mRNA
FEATURE:
NAME/KEY: 5'UTR
LOCATION: 1..393
FEATURE:
NAME/KEY: CDS
LOCATION: 394..1389
FEATURE:
NAME/KEY: 3'UTR
LOCATION: 1390..1671
US-08-706-281A-15

Query Match 47.3%; Score 939; DB 3; Length 1671;
Best Local Similarity 79.4%; Pred. No. 2.9e-219;
Matches 1249; Conservative 0; Mismatches 304; Indels 20; Gaps 11;

| | | | | |
|---------|-------|--|------|--|
| Matches | 12457 | CONS | 2000 | |
| Qy | 144 | AAAAAAGAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAGCAAAAGAGCAGACTCTTT | 203 | |
| Db | 94 | AATGCATAAGATTAAAGTTAAAGCAGAAGTGAGAACAAGAAAGCAAGAGCAGACTCTTT | 153 | |
| Qy | 204 | GAACTAAGAATGAGCATTTCAGAAATCGAAGATGTTACAGTGAAGGTGATCGGGAGCTGTA | 263 | |
| Db | 154 | CAACTGAGAATGAATATTTT-GAAGCCCAAGATTTTAACTGTATGATGATTAGAGTCGTA | 212 | |
| Qy | 264 | CCTGGAAGACAGTAAGAGCTCCACTGCCAGCCTTTTGAGGACACGGGACAGGTACTCAACA | 323 | |
| Db | 213 | CCTAAAAGAGACTAAAAACTCCATGTCAAGC---TCTGGACTTGTGACATTACTC-ACA | 268 | |
| Qy | 324 | CCTGGCAGGCCAGCTGGATCCTCAGAACTTTGGGACGCACGGAGAGGGGGAGAATCAC | 383 | |
| Db | 269 | GCAGGCATGGCAATTTTAGCCTCACAACCTTTCAGACAGATAAAGACTTGAGGAAATAAC | 328 | |
| Qy | 384 | CG---GGGCTCCCTGGCTGGAGAGGCCGAATCAGTCCCGAGGGGGTCTGCATACACTTGT | 440 | |
| Db | 329 | TGAGACGACTCCCTGACCCAGGAGGTAAATCAATTGAGGGGACACTGGA-ATTCTCCT | 387 | |
| Qy | 441 | TGCAGGATGAACTCCACCTTCAGCACGGAATGCACACTTCTCTCCACTTCTGGAACCGC | 500 | |
| Db | 388 | GCCAGCATGGTGAATCCACCCACCGTGGGATGCACACTTCTCTGCACCTCTGGAACCGC | 447 | |
| Qy | 501 | AGCACCTACGGACAGCACGGCAACGCCACTGAGTCCCTTGCCAAAGGCTACCCGACGGG | 560 | |
| Db | 448 | AGCAGTTACAGACTGCACAGCAATGCCAGTGAGTCCCTTGGAAGGCTACTCTGATGGA | 507 | |
| Qy | 561 | GGATGCTACGAGCAACTCTTCGTCTCCCGGAGGTGTTCTGTGACTCTGGGGTGCATAAGC | 620 | |
| Db | 508 | GGGTGCTACGCGCAACTTTTGTCTCTCTGAGGTGTTGTGACTCTGGGTGTGATCAGC | 567 | |
| Qy | 621 | TTGCTGGAGAACATTTCTGGTGATCGTGGCAATAGCCAAGAACAAGAAATCTGCACTCACCC | 680 | |
| Db | 568 | TTGTTGGAGAATATCTTAGAGATTGTGGCAATAGCCAAGAACAAGAAATCTGCATTACCC | 627 | |
| Qy | 681 | ATGTACTTTTTTCATCTGTAGCCTGGCTGTGGCCGATATGCTGGTGAGCGTTTCCAACGGG | 740 | |
| Db | 628 | ATGTACTTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGCTGGTGAGCGTTTCAAATGGA | 687 | |

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Sequence alignment: WO/00/27863

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AA26972;
XX
DT      04-AUG-2000   (first entry)
XX
DE      Rhesus monkey melanocortin-4 receptor gene.
XX
KW      Rhesus monkey; rhodopsin; G-protein coupled receptor; anorectic;
KW      melanocyte stimulating hormone; melanocortin receptor; obesity; ss.
XX
OS      Macaca mulatta.
XX
FH      Key           Location/Qualifiers
FT      CDS            17..1015
FT                        /*tag= a
FT                        /product= "melanocortin-4 receptor protein"
XX
PN      WO200027863-A1.
XX
PD      18-MAY-2000.
XX
PF      05-NOV-1999;   99WO-US25767.
XX
PR      09-NOV-1998;   98US-0107721.
XX
PA      (MERI ) MERCK & CO INC.
XX
PI      MacNeil DJ, Weinberg DH, Van Der Ploeg LHT;
XX
DR      WPI; 2000-376480/32.
DR      P-PSDB; AAY94301.
XX
PT      Novel DNA encoding rhesus monkey melanocortin 4 receptor protein,
PT      recombinant,vectors and host cells, useful in methods for identifying
PT      selective agonists and antagonists -
XX
PS      Claim 1; Page 35; 53pp; English.
XX
CC      The present sequence encodes the rhesus monkey melanocortin-4
CC      receptor protein (MC-4R). Melanocortin receptors belong to the
CC      rhodopsin sub-family of G-protein coupled receptors. They bind and are
CC      activated by peptides such as alpha-, beta-, or gamma-melanocyte
CC      stimulating hormones derived from the pro-opiomelanocortin gene and they
CC      are believed to mediate a wide range of physiological functions.
CC      The rhesus MC-4R gene was isolated by PCR using a series of four
CC      oligonucleotides (AAA26973-A26976) based on the human MC-4R gene sequence
CC      and designed to incorporate a restriction enzyme site for cloning into
CC      the expression vector pCI-neo. The recombinant vector was transformed
CC      into DH5a cells in preparation for DNA sequencing. The present sequence
CC      or a mutated form may be introduced into an expression vector for
CC      expression in host cells. The subcellular membrane fractions will
CC      comprise either wild-type or mutant forms of rhesus MC-4R at enhanced
CC      levels and can be used in assays to identify ligand binding, activators
CC      and modulators, agonists and antagonists of MC-4R. This will allow for
CC      selection of compounds that are active for the rhesus receptor in vitro
CC      and will allow the selection of novel drugs to treat obesity.
XX
SQ      Sequence 1030 BP; 239 A; 254 C; 222 G; 315 T; 0 other;

Query Match          41.2%; Score 817.6; DB 21; Length 1030;
Best Local Similarity 87.4%; Pred. No. 8.8e-184;
Matches 895; Conservative 0; Mismatches 129; Indels 0; Gaps 0;

Qy      436 CTTGTTGCAGGATGAACCTCCACCCTTCAGCACGGAATGCACACTTCTCTCCACTTCTCGGA 495
Db              ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Qy      496 ACCGCAGCAGCTACGGACAGCACGGCAACGCCACTGAGTCCCCTGGCAAAGGCTACCCCCG 555
Db              ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Qy      66 ACCGCAGCAGCCACAGACTGCACAGCAATGCCAGTGAGTCCCCTGGAAAAGGCTACTCTG 125
Db              ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Qy      556 ACGGGGGATGCTACGAGCAACTCTTCGTCTCCCCGGAGGTGTTTCGTGACTCTGGGGGTCA 615
Db              ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||
Qy      126 ATGGAGGGTGCTACGAGCAACTTTTGTCTCTCTGAGGTGTTTGTGCACTGGGTGTCA 185
Db              ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| ||| |||

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